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LETTER TO THE EDITOR

IN RESPONSE TO: "BREAST IMPLANT ASSOCIATED ANAPLASTIC LARGE CELL LYMPHOMA DEVELOPMENT CASE IN A SET OF DIZYGOTIC TWINS WITH BREAST IMPLANTS"

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Dear Editor,

We have read with great interest the paper titled "Breast Implant Associated Anaplastic Large Cell Lymphoma development case in a set of dizygotic twins with Breast Implants" by Latini and colleagues [1], reporting a case of BIA-ALCL in a set of dizygotic twins, one of whom developed BIA-ALCL infiltrating beyond the capsule (pT4), while her sibling was negative for the disease despite developing similar symptoms ultimately leading to implant removal.

The first of the two twins underwent implant substitution with total capsulectomy 22 years after breast augmentation and 4 years after the development of a nonspecific inflammatory nodule and symptomatic breast effusion. She was diagnosed as BIA-ALCL pT4, infiltrating beyond the capsule, breast implants were removed, free surgical margins were achieved and staging revealed no distant metastasis (Stage IIA). She is currently in follow-up. The twin sister developed similar symptoms, including breast swelling and hardening, but no periprosthetic effusion on breast ultrasound, 11 years after breast augmentation. She underwent implant replacement, total capsulectomy and histologic evaluation did not reveal BIA-ALCL. Nonetheless they found abundant chronic histiocytic inflammation bilaterally and a mosaic karyotype aberrations 47 XXX/46 XX in capsule fragments. To date the second sister has not developed BIA-ALCL.

The Authors state that no convincing evidence currently exists regarding the possibility of genetic predisposition and/or familial inheritance, wishing further investigations and research on the possible genetic predisposition for BIA-ALCL. Building upon these considerations, we would like to introduce our own recent research, in which we discuss the genetic factors predisposing to the development of BIA-ALCL [2]. We reported a case of BIA-ALCL in a patient with known germline BRCA 1 mutation and we systematically reviewed the literature regarding genetic factors predisposing to BIA-ALCL.

De Boer et al. in 2020 [3] estimated the absolute risk of developing BIA-ALCL in female carriers of BRCA1/2 mutations to be around 1/1,551 before the

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age of 75, compared to 1/ 7,507 of non-carriers. Also Santanelli et al. [4] in 2022 observed an increased risk of developing BIA-ALCL in BRCA1/2 mutation carriers or in women affected by Li-Fraumeni syndrome compared to general population. A case of BIA ALCL in a patient carrying a pathogenic mutation of PALB2 was described by Bonev et al. [5] and Tevis et al. [6] discovered a significant difference in HLA A*26 allele frequencies between BIA-ALCL patients and the general population.

Genetic factors predisposing to the development of BIA-ALCL may explain the higher prevalence of the disease in specific subpopulations of women with genetic risk factors for breast cancer compared to the general population and may also explain some geographical differences in BIA-ALCL prevalence. BIA-ALCL cells possess a specific pattern of genetic alterations, mainly including JAK-STAT, DNMT3A, PD-L1 chromosomal copy number aberrations (CNAs), chromosome 20q loss, (CA9) overexpression, TP53 mutations [7].

The hypothesis is that a dysregulation of the JAK1/STAT3 pathway may occur in genetically susceptible patients, predisposing the emergence and proliferation of CD30+ monoclonal and ALK-negative cells in response to inflammatory/irritative stimuli caused by the implant [7,8].

The management of BIA-ALCL in women with genetic predisposition for breast cancer is similar to that of non-mutation carriers. According to the most recent guidelines for diagnosis and treatment of BIA-ALCL [9], as soon as a confirmed diagnosis of BIA- ALCL is made on fluid, periprosthetic capsule, mass or lymph node, a positron emission tomography (PET/CT) should be planned preoperatively to stage the disease. An en-bloc capsulectomy is required as the gold standard procedure in case of disease confined to the fluid around the implant and/or the capsule. In cases of locally advanced disease with the presence of a mass or chest wall infiltration, a multidisciplinary evaluation is required to set up therapeutic modalities, including en-bloc capsulectomy along with the removal of the mass with free margins, adjuvant chemo-immunotherapies (Brentuximab Vedotin plus cyclophosphamide, doxorubicin, prednisone) [10] and eventually locoregional radiotherapy. After appropriate treatment, tailored to disease staging, the patient should perform a clinical-radiological follow-up every 3-6 months for the first 2 years and afterwards, annual evaluations up to 5 years.

Even in case of genetic predisposition and/or familial inheritance, no data currently support the preventive removal of macrotexture implants in asymptomatic women [11]. There is no evidence in literature that suggests that a complete capsulectomy in asymptomatic patients reduces the risk of BIA-ALCL [12]. In addition, according to current knowledge, breast reconstruction with microtextured or smooth implants can be offered to women with a genetic predisposition for breast cancer and requiring risk-reducing surgery, as well as autologous reconstructions (flaps or fat grafting) when available.

In conclusion the paper presented by Latini et al. provides interesting cues into the topic of genetic predisposition to BIA-ALCL and we would like to point out that some evidences in this regard do exist in the literature. We fully agree with the Authors that further research is needed to better understand the etiopathogenesis of the disease and to develop new therapeutic and preventive strategies once able to identify those patients possessing susceptible genetic profiles.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

RC: A, W
FD: A, W
LM: DT

Abbreviations

A: conceived and designed the analysis
D: collected the data
DT: contributed data or analysis tool
S: performed the analysis
W: wrote the paper
O: other contribution (specify contribution in more detail)

Ethical consideration

Not applicable.

References

1 Latini C, Castrechini M, Pedace D, et al. Breast implant associated-anaplastic large cell lymphoma development case in a set of dizygotic twins with breast implants. PRRS 2023;2:7-11. https://doi.org/10.1038/s41379-018-0134-3

2 Carbonaro R, Accardo G, Mazzocconi L, et al. BIA-ALCL in patients with genetic predisposition for breast cancer: our experience and a review of the literature. Eur J Cancer Prev 2023;32:370-376. https://doi.org/10.1097/CEJ.0000000000000809

3 de Boer M, Hauptmann M, Hijmering NJ, et al. Increased prevalence of BRCA1/2 mutations in women with macrotextured breast implants and anaplastic large cell lymphoma of the breast. Blood 2020;136:1368-1372. https://doi.org/10.1182/blood.2019004498

4 Santanelli Di Pompeo F, Panagiotakos D, et al. BIA-ALCL epidemiological findings from a retrospective study of 248 cases extracted from relevant case reports and series: a systematic review. Aesthet Surg J 2023;43:545-555. https://doi.org/10.1093/asj/sjac312

5 Bonev V. A case report of breast implant-associated anaplastic large-cell lymphoma in a PALB2 mutation-positive woman. Am Surg 2021;Apr 15. https://doi.org/10.1177/00031348211011056 [Epub Ahead of Print]

6 Tevis SE, Hunt KK, Miranda RN, et al. Differences in human leukocyte antigen expression between breast implant-associated anaplastic large cell lymphoma patients and the general population. Aesthet Surg J 2019;39:1065-1070. https://doi.org/10.1093/asj/sjz021

7 Wang Y, Zhang Q, Tan Y, et al. Current progress in breast implant-associated anaplastic large cell lymphoma. Front Oncol 2022;11:785887. https://doi.org/10.3389/fonc.2021.785887

8 Laurent C, Nicolae A, Laurent C, et al. Gene alterations in epigenetic modifiers and JAK-STAT signaling are frequent in breast implant-associated ALCL. Blood 2020;135:360-370. https://doi.org/10.1182/blood.2019001904

9 Longo B, Di Napoli A, Curigliano G, et al. Clinical recommendations for diagnosis and treatment according to current updated knowledge on BIA-ALCL. Breast 2022;66:332-341. https://doi.org/10.1016/j.breast.2022.11.009

10 Horwitz S, O'Connor OA, Pro B, et al. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): a global, double-blind, randomised, phase 3 trial. The Lancet 2019;393:229-240. https://doi.org/10.1016/S0140-6736(18)32984-2

11 The ANSM decides, as a precautionary measure, to withdraw from the market macrotextured breast implants and breast implants with polyurethane-coated surfaces. Medical Device Expert News [cited 2023;Oct 13] (Available from: https://www.medicaldevice.expert/europe/france/agence-nationale-de-securite-du-medicament/the-ansm-decides-as-a-precautionary-measure-to-withdraw-from-the-market-macrotextured-breast-implants-and-breast-implants-with-polyurethane-coated-surfaces).

12 Breast implants – certain labeling recommendations to improve patient communication. FDA [Internet]. [cited 2023;Oct 13] (Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breast-implants-certain-labeling-recommendations-improve-patient-communication).

REPLY: BREAST IMPLANT ASSOCIATED ANAPLASTIC LARGE CELL LYMPHOMA DEVELOPMENT CASE IN A SET OF DIZYGOTIC TWINS WITH BREAST IMPLANTS

Dear Editor,

We read the paper from Carbonaro et al. [1] with great pleasure, and while we appreciated their critical appraisal of our work [2], we could not help but reflect on one of your closing statements. Indeed, the management of symptomatic patients with Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) has been well established [3].

However, we cannot find ourselves in agreement with the point in which the authors stated that no data currently support the preventive removal of macrotextured implants in asymptomatic patients.

In fact, they referenced a paper from Santanelli di Pompeo et al. [4] which correlated certain germline mutations for increased risk of BIA-ALCL onset. However, our reading of said work suggested even deeper ramifications. In fact, the systematic review of literature from 248 case reports in literature used Kaplan-Meier survival curves and correlation statistics to also demonstrate the effect of implant replacement in asymptomatic patients, showing for the first time in literature that this procedure had protective role against BIA-ALCL onset. Additionally, what we found astounding is how these findings were independently replicated in another study by Vittorietti et al. [5] where 232 BIA-ALCL cases extracted from literature were also assessed for quantitative analysis. In fact, they also found that that implant substitution and/or capsulectomy may delay the BIA-ALCL onset. Such evidence deserves to be evaluated critically because of relevant limits such as the fact that the studies were only based on case reports or case series, in a retrospective nature, inherently lowering the level of evidence. Even so, these studies were the first of their kind to demonstrate a protective role of implant replacement reducing BIA-ALCL risk of occurrence.

However, there are still questions and uncertainties regarding the role of capsulectomies in BIA-ALCL prevention. Of note, there is a clear lack of cohesiveness in the definitions used to address capsulectomy types [6], and there are questions regarding the potential risks of morbidity or even mortality [7,8]. Therefore, according to our understanding, the removal/replacement of macrotextured implants has only been suggested by the current evidence with a relative indication, that should be determined on a patient-to-patient basis as determined by the clinicians and their patients, by stratifying their risk.

We believe that indeed more evidence is need, particularly in terms of prospective studies, to ascertain the utility of capsulectomies, potentially with a quantitative assessment of risk-benefit ratios. And, in the light of all the above considerations, we truly thanks the Carbonaro et al. for the considerable reflections sent to our attention.

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References

1 Carbonaro R, Mazzocconi L, De Lorenzi F. In response to: "Breast implant associated anaplastic large cell lymphoma development case in a set of dizygotic twins with breast implants". PRRS 2023;2:104-106. https://doi.org/10.57604/prrs-366

2 Latini C, Castrechini M, Pedace D, et al. Breast implant associated-anaplastic large cell lymphoma development case in a set of dizygotic twins with breast implants. PRRS 2023;2:7-11. https://doi.org/10.57604/prrs-100

3 Asaad M, Offodile AC, Santanelli Di Pompeo F, et al. Management of symptomatic patients with textured implants. Plast Reconstr Surg 2021;147:58S-68S. https://doi.org/10.1097/PRS.0000000000008047

4 Santanelli Di Pompeo F, Panagiotakos D, et al. BIA-ALCL Epidemiological findings from a retrospective study of 248 cases extracted from relevant case reports and series: a systematic review [published correction appears in Aesthet Surg J 2023 Feb 22]. Aesthet Surg J 2023;43:545-555. https://doi.org/10.1093/asj/sjac312

5 Vittorietti M, Mazzola S, Costantino C, et al. Implant replacement and anaplastic large cell lymphoma associated with breast implants: a quantitative analysis. Front Oncol 2023;13:1202733. Published 2023;Oct 19. https://doi.org/10.3389/fonc.2023.1202733

6 Gerzenshtein J. The dishonesty of referring to total intact capsulectomy as "En Bloc" resection or capsulectomy. Plast Reconstr Surg 2020;145:E227-E228. https://doi.org/10.1097/PRS.0000000000006362

7 Abi-Rafeh J, Safran T, Winocour S, et al. Complications of capsulectomies: an analysis of the American College of Surgeons National Surgical Quality Improvement Program Database. Aesthet Surg J Open Forum 2022;4:ojac025. Published 2022;Apr 12. https://doi.org/10.1093/asjof/ojac025

8 Santanelli di Pompeo F, Sorotos M, Clemens MW, et al. Mortality rate in breast implant surgery: is an additional procedure worthwhile to mitigate BIA-ALCL risk? Aesthetic Plast Surg 2023;47:914-926. https://doi.org/10.1007/s00266-022-03138-5